TITLE:

Attitudes towards antenatal vaccination, Group B streptococcus and participation in clinical trials: Insights from focus groups and interviews of parents and healthcare professionals

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CONFLICTS OF INTEREST

MDS has participated in advisory boards and/or been an investigator on clinical trials of vaccines sponsored by vaccine manufacturers including Novartis Vaccines, GlaxoSmithKline, Pfizer, Crucell and Sanofi Pasteur. Payment for these services was made to the University of Oxford, Department of Paediatrics. MDS has had travel and accommodation expenses paid to attend conferences by Novartis Vaccines and GlaxoSmithKline. MDS has received no personal payment from vaccine manufacturers. JP is the Chief Executive of Group B Strep Support, a charity which offers support and information to families affected by Group B strep, informs health professional about the prevention of Group B strep infection and supports research into to preventing these infections in new-born babies. The remaining authors have no potential conflicts of interest to declare.

ABSTRACT

INTRODUCTION

Antenatal vaccination has become a part of routine care during pregnancy in the UK and worldwide, leading to improvements in health for both pregnant women and their infants. However, uptake remains sub-optimal. Other antenatal vaccines targeting major neonatal pathogens, such as Group B streptococcus (GBS), the commonest cause of sepsis and meningitis in the neonatal period, are undergoing clinical trials but more information is needed on how to improve acceptance of such vaccines.

METHODS

Qualitative study using focus groups and interviews; involving 14 pregnant women, 8 mothers with experience of GBS, and 28 maternity healthcare professionals. Questions were asked regarding antenatal vaccines, knowledge of GBS, attitudes to a potential future GBS vaccine and participation in antenatal vaccine trials.

RESULTS

All participants were very cautious about vaccination during pregnancy, with harm to the baby being a major concern. Despite this, the pregnant women and parents with experience of GBS were open to the idea of an antenatal GBS vaccine and participating in research, while the maternity professionals were less positive. Major barriers identified included lack of knowledge about GBS and the reluctance of maternity professionals to be involved.

INTERPRETATION

In order for a future GBS vaccine to be acceptable to both pregnant women and the healthcare professionals advising them, a major awareness campaign would be required with significant focus on convincing and training maternity professionals.

KEYWORDS

Group B streptococcus, antenatal vaccine, pregnancy, attitudes, healthcare professionals, pregnant women, clinical trials

INTRODUCTION

Group B streptococcus (GBS, also known as *Streptococcus agalactiae*) is the commonest cause of sepsis and meningitis in the first three months of life (1-4). The incidence appears to be increasing (3, 4) and mortality is around 10%, with about half of babies who recover from GBS meningitis left with long term neurodevelopmental sequelae (5).

Around 14-30% of UK women carry GBS in their gastrointestinal or genital tract (6-8) and without prophylaxis around 1% of babies born to these women will develop invasive GBS infection (6-8). The majority of early-onset infections (occurring from 0-6 days of life) can be prevented by administration of intravenous Benzylpenicillin to the mother during labour (9, 10), but this does not prevent the less common late-onset disease (7-90 days of life) (10, 11) and a major challenge is identifying which women should receive these intrapartum antibiotics. The UK currently uses a risk-based approach in which women with known risk-factors are given antibiotics but are not tested for GBS carriage (12). This differs from the USA, Australia and many European countries where women are predominantly offered screening for GBS during the later stages of pregnancy and are given antibiotics during labour if their test is positive (13, 14).

Neither strategy is ideal. The risk-based approach may miss a significant proportion of colonised women (7, 15, 16) and since its introduction, GBS rates in the UK have continued to rise (3), while countries adopting a screening policy have seen a significant fall (11). However, screening programs also face multiple issues including sub-optimal uptake, and potentially greater antibiotic use (4, 17). Neither strategy impacts on prenatal or late-onset infection.

Therefore, the prospect of an antenatal vaccine, which could be given to all women during pregnancy and would likely protect against both prenatal, early- and late-onset disease, is an

attractive option. At present there is no licenced GBS vaccine; however, clinical trials have shown promising initial results (18) and larger scale studies are ongoing (NCT02459262).

One potential challenge facing the introduction of a GBS antenatal vaccine is that in order for a vaccine to be effective, it must be accepted by both the target population, namely pregnant women, and the healthcare professionals caring for them. In the UK, two antenatal vaccines are recommended; influenza and pertussis (19). However, despite the increasing level of evidence that these vaccines are both safe and effective (20, 21), uptake rates remain low – approximately 60% for pertussis (22) and only 38.3% for influenza (23).

This qualitative study was conducted as part of a larger project with the overall aim of obtaining more in-depth information on the attitudes and opinions of pregnant women and healthcare professionals towards antenatal vaccination, GBS, a potential GBS vaccine and participation in clinical trials during pregnancy, which were prominent issues raised during an initial large-scale survey of British women of child-bearing age (24, 25).

METHODS

This qualitative study was conducted in Spring 2014 and approved by the NRES ethics committee South Central- Hampshire A (Ref 13/SC/0619).

Participants

There were three categories of participant; 14 pregnant women, 8 women with experience of their own child being affected by GBS infection and 28 maternity professionals (10 midwives and 18 obstetric doctors). Further details are given in tables 1 and 2.

Pregnant women were recruited using participant information booklets/invitations sent with their ultrasound appointment letter. These appointment letters are sent to all pregnant women

upon informing their GP/midwife of their pregnancy. Maternity professionals were recruited through adverts at educational meetings, on staff newsletters and in staffrooms. Of note, all participants and maternity staff were receiving antenatal care/working within the publically funded UK National Health Service. This is typical for antenatal care in the UK where only 0.4% of women receive exclusively private maternity care (26). The recruitment area (Oxford University Hospital NHS Trust) includes all levels of maternity care from community home birth services to a high-risk regional referral unit. Parents who previously had a child with GBS infection responded to an advert in the Group B Strep Support newsletter. All participants were offered a £20 shopping voucher to compensate for their time.

Inclusion criteria were that all participants were over 18 years of age, able to speak and understand English, able to give informed, written consent and lived within one-hour travel distance or were able to travel themselves to the study site (Oxford, UK). All parents in the GBS experienced group had a child affected by GBS infection. Maternity professionals were required to be midwives or obstetric doctors currently working within the Oxford University Hospitals NHS Trust. Participation was voluntary and participants were allowed to withdraw at any point without giving a reason.

Due to the sensitive nature of their previous experience, women with experience of GBS took part in individual interviews only, while pregnant women were allocated, based on their availability, to take part in either interviews or focus groups. A decision was made to conduct focus groups only amongst the maternity professionals to reflect the normal working environment in which views and practice are influenced by discussion with colleagues and hospital or national policy. To avoid any sense of inter-professional hierarchy, focus groups contained participants of the same discipline (e.g. either midwives, or obstetric doctors).

Interviews and focus groups topic guides

Topic guides for both the interviews and focus groups were developed after a review of the literature, and using data and themes obtained from a previous online survey (24, 25). As previous research had shown a general low level of knowledge about GBS (24), a GBS fact sheet was provided during the interviews/focus groups with details on incidence, mortality, screening and current status of a GBS vaccine.

The topic guides were piloted in two interviews (one with a pregnant women and one with a GBS experienced parent) and minor adjustments were made based on the feedback obtained.

Conduct of the interviews/focus groups

Informed, written consent was obtained before the start of each interview or focus group. All interviews were conducted face-to-face by a qualitative researcher, in either their own home or at the study site. Focus groups took place at either the study site offices or the hospital (for maternity professionals) and were led by the same researcher with a clinical member of the study team in order to clarify technical questions raised by the group. All interviews and focus groups were audio recorded.

Analysis

All recordings were transcribed verbatim and a thematic framework analysis was conducted using NVIVO 10 software, structured around the main areas of questioning. Data analysis and data collection proceeded iteratively and early findings informed questioning in the subsequent interviews and focus groups until theoretical saturation was felt to be achieved. The content of focus group discussions was similarly analysed by theme, but with additional analysis of the interactions between focus group members in each case, and how this affected the content. Where relevant we report these interactive aspects in the findings.

RESULTS

General attitudes towards vaccines

A range of views were expressed regarding vaccinations, with most women focussing on the context of childhood vaccination. Some were strongly supportive;

"I think it's a brilliant idea and I think you'd be mad not to do it to be honest." (Pregnant women 0002)

While others were more hesitant,

"I'm like ambivalent, so I, I would prefer to live in a world where we don't need vaccines." (Pregnant women 0012)

However, the overarching theme was a general acceptance of childhood vaccines, as this was perceived as the norm and the majority of childhood vaccines had been around for a long time. Key influences included the attitudes of the women's own parents towards vaccination, and the perceived risk-benefit ratio with the severity of the condition being more important than how common it was. There was general perception that vaccines themselves may carry a risk, some women spoke about the MMR-Autism debate or media concerns about the Swine flu vaccine, nevertheless, the risk of not having the vaccine was often felt to be greater.

Vaccination during pregnancy

In contrast to routine childhood vaccination, pregnant women were much more cautious about receiving vaccines while pregnant, with a major concern being potential harm to their baby.

"I guess it's a little bit more scary, so it's sort of fair enough when you've got to have your own vaccine as an adult because, you kind of, are making that choice.... But I guess it's a

little bit more of an unknown when you're pregnant because you do worry about is it going to affect the baby in a negative way." (Pregnant woman 0002)

Despite these anxieties, many of the women interviewed had received the flu vaccine and/or intended to have the pertussis vaccine, the main influence being a recommendation either nationally or from a healthcare provider. Some expressed specific worries about the influenza vaccine being recommended in the first trimester, advice which had changed since previous pregnancies, and commented that they would prefer to have it later as this was perceived as safer and at this point the symptoms of early pregnancy would have resolved.

The concept of the vaccines being introduced as a result of scientific research was mentioned by a number of women, though few had considered the specifics of this research, such as the size of the clinical trials or length of follow up, and assumed that vaccines were being recommended based on good evidence. Midwives and other healthcare professionals were viewed as important sources of reliable information, though many would also discuss with their partner and pregnant friends.

The midwives and obstetric doctors also echoed the pregnant women's cautious attitude towards vaccination during pregnancy and commented on the challenge of practice changing recently, from advising no medications or vaccines during pregnancy to promoting antenatal vaccination. Several raised concerns about the number of vaccines, "the cocktail", now recommended and the possibility of long term effects. In keeping with this, some wanted clinical trials to follow-up outcomes for 15-20 years or even two generations. The existence of a national recommendation was key for them and, while they also spoke about the important of research, many had not looked into the details themselves and, in a similar way to the pregnant women, trusted in the 'official', 'NHS' guidance.

Awareness of GBS and attitudes towards a GBS vaccine

Awareness of GBS in the pregnant women group was low. Both the pregnant women and the GBS experienced group felt that large-scale awareness campaigns, similar to those targeting meningococcal disease, were needed. The word ‘meningitis’ was felt to resonate strongly with the general population and if people were aware that GBS could cause meningitis this would indicate it was a dangerous condition. Those with experience of GBS were particularly keen that information was given early in pregnancy, as they had not received it themselves.

The pregnant women were generally supportive of a GBS vaccine, particularly after receiving additional information about GBS, with the potential mortality being a key factor. Unsurprisingly, the GBS experienced group were strongly in favour of a vaccine. Offering the vaccine to all pregnant women rather than using a screening approach was seen as a positive aspect for both of these groups,

“It’s a lot neater being given a vaccine and it’s less open to error in terms of how it’s administered because at the moment the NICE guidelines are very complicated and medical professionals don’t understand them and people fall through the gaps like I did.” (GBS experienced group 1009)

The majority of pregnant women felt they would want to know more facts about the vaccine and GBS in general, for which midwives were considered to be the authoritative source of information. Those with experience of GBS also highlighted the need for better information, but in their experience, maternity staff and GPs were often not very well informed.

In contrast, the midwives in the first focus group were less positive about a potential GBS vaccine, with cost-effectiveness and the safety of the vaccine being major concerns given the relatively few deaths from GBS in the UK. Some felt that screening would be more in keeping with the ‘natural’ approach favoured by midwifery culture,

‘I suppose as a midwife my heart is more for screening than putting something into women that they don’t need to have. I want to try to pick up a really good screening tool’.

(Midwife, focus group 1)

One midwife, who had personal experience of looking after a mother whose baby had died of GBS, consistently tried to challenge this view, however, the other participants remained unconvinced and viewed her story as a one-off case. Nevertheless there was a discussion about keeping an open-mind. The midwives in the second focus group, one of whom had experienced cases of babies dying from GBS in her clinical practice, were more in favour of a vaccine. The obstetric doctors were also more willing to consider a GBS vaccine and argued that vaccination could be more cost-effective than treating the consequences of GBS infection.

Participation in GBS vaccine research

Many of the pregnant women were open to the idea of participating in clinical trials of vaccine research but were generally very cautious, felt they would need more information and would be less likely to take part if it were their first pregnancy.

“I suppose I’d want to know more about it at that stage then, you know, I would want more than a leaflet I think, if I was actually going to take part in a trial.”

(Pregnant woman 002)

The GBS experienced group were very positive about research.

“If I was going to fall pregnant again I would, I would volunteer. I would probably give you my arm now so you could happily give it *(the GBS vaccine)* to me. I would be more than happy to because I know the consequences”

(GBS experienced group 1008)

Suggested methods of encouraging pregnant women to take part are listed in table 3. While travel and childcare expenses were seen as essential, a monetary payment for taking part was not felt to be a strong motivator by the pregnant women. The concept of being part of a control group, who did not receive the vaccine, was attractive to some, as they could contribute to the research without feeling they were putting their baby at risk.

The maternity professionals groups were less keen on being involved and while some might consider distributing information about the trial, they would not want to be seen to be recommending it unless they could be convinced of the vaccine safety. They acknowledged that this ambivalence could be a major obstacle to recruitment. In contrast to the cautiously positive responses from the pregnant women, the second obstetric doctors' focus group questioned whether a GBS vaccine trial would even be feasible due to women willing to take part.

INTERPRETATION

These data provide interesting insight into the attitudes of pregnant women, women with experience of GBS and maternity professionals, regarding antenatal vaccination. Overall, pregnant women and maternity professionals were typically cautious but accepting of the current recommended antenatal vaccines. Pregnant women and those with experience of GBS were generally supportive of a possible GBS vaccine and participating in research while the maternity professionals were more sceptical, with the notable exception of those who had direct experience of GBS. There was a clear difference in attitudes between childhood vaccinations and vaccines offered during pregnancy. Childhood vaccinations were perceived as the default option and even vaccine-hesitant parents had decided to have their children

vaccinated. A key factor in this seemed to be the perceived length of time these vaccines had been in use and pregnant women were able to reference their own experiences as children and the influence of their own parents on their decisions to vaccinate. On the other hand, the introduction of antenatal vaccination in the UK, initially with vaccination against swine flu, then seasonal influenza in 2010 followed by pertussis in 2012 (19), came on the background of a strong prevailing culture that no unnecessary medications should be given during pregnancy and this seemed to strongly influence both the pregnant women and maternity professionals. This may change and evolve with time - in many developing countries, maternal immunization to prevent neonatal tetanus has been ongoing for many years and coverage rates are significantly higher, reaching 80-90%, in some countries (27, 28).

Although both pregnant women and midwives expressed concerns, it is important to note that women were engaged in working out how to fulfil a socially expected role of 'good motherhood', in which the focus is not just on them but also on their responsibility to protect their unborn child. For women, risk may be primarily perceived at a personal level – if your baby gets GBS, population statistics may feel irrelevant and almost any strategy to avoid potential major harm may seem desirable. There was some evidence in women's accounts of a general sense of pressure to do or not do things in pregnancy without really understanding why. This could be considered a manifestation of 'reproductive citizenship', whereby pregnant women and their fetuses become 'potent focal points for regulation, monitoring and control' (29) and the fetus 'is privileged over the pregnant woman….eclipsing the maternal body in which it grows' (29). However, in the specific case of GBS and a GBS vaccine, women in our sample presented this in more proactive terms of their own agency, wanting to be informed about how to protect their baby, and thereby protect themselves from the grief of neonatal loss, and seeing it as a positive opportunity rather than irksome surveillance or control. This may be at odds with midwives' perception of GBS as a very small collective

risk, informed by professional norms of pregnancy as a safe, normal and healthy process. Thus women's threshold for weighing up the risk/benefit ratio comes from a very different perspective. It is significant that the midwives who themselves had encountered GBS in their own practice saw risk through a similar lens as the women.

Providing information about both the vaccines and the diseases they prevent has been shown to be key (30) and this was echoed by all groups in this study. Pregnant women looked to their healthcare professionals, particularly midwives, for advice; however, the healthcare professionals often echoed their concerns, despite the increasing evidence that antenatal vaccination is both safe and effective (20, 21, 31, 32). However, some of the healthcare workers who had received additional vaccine-related training were more positive and keen to educate their colleagues. Addressing the ideas and concerns about antenatal vaccination amongst maternity professionals could therefore be key in promoting antenatal vaccine uptake.

Encouragingly, pregnant women and the GBS experienced group were generally in favour of GBS vaccine. They highlighted comparable ideas and concerns to those expressed in a similar qualitative study conducted in Canada (33). However, an important difference is that GBS screening is routine in Canada and interestingly, the healthcare professionals, with their experience of screening, were very much in favour of vaccination as an alternative. This contrasts with the views expressed by many of the professionals participating in this study, some of whom preferred the possibility of a screening approach. Our data also suggest that while the target population of pregnant women may be open to the idea of taking part in clinical trials, a major obstacle could be the attitudes of the healthcare professionals and significant work must be undertaken to persuade this key group. In the maternity professionals' focus groups, the influence of collective professional norms was strongly in

evidence, with any dissenting voices, such as the midwife with experiences of GBS, being regarded as less relevant by the others.

Qualitative studies are designed to elicit a range of perspectives, rather than to be statistically representative, so while we have uncovered important themes to consider, if a vaccine is to be implemented effectively, we cannot conclude how common these attitudes and concerns are in the whole patient or professional population. We also cannot determine whether those volunteering to participate truly represent the population of interest, however our recruitment methods aimed to give as wide a range as possible the opportunity to take part. Focus groups were selected because they reflect the reality of how professional staff culture works and how women form views about topics in pregnancy. However, a limitation of focus groups is that participants may have felt obligated to go along with the current hospital/national policies and despite the attempts to minimise the effects of hierarchy, more junior members of the group may have felt less able to contribute. Conducting individual interviews may have removed some of these barriers, but would have been less effective in examining how decisions and consensus are reached in the workplace setting. As Kitzinger (34) argues, much of what we learn in life is acquired by talking and observing in groups; if we want to explore people's understandings, 'it makes sense to employ methods which actively encourage examination of these social processes in action'.

With these limitations in mind, the depth of responses and emerging themes from this study have aided the development of a questionnaire, which has since been used for a large scale national survey of pregnant women and healthcare workers (35). Altogether, this project identified key issues which need to be addressed and potential strategies which can help prepare the UK for an effective GBS vaccine.

Table 1: Pregnant women and women with experience of GBS

Group	Number of participants	Age range	Participant characteristics
Pregnant women	14	21-41 years	• First pregnancy: 5 • Second pregnancy: 7 • Third pregnancy: 1 • Unspecified: 1
Women with experience of GBS	8	25-45 years	• 1 child affected: 6 • 2 children affected: 2 • Child alive and well: 5 • Child died: 4 • Child with ongoing problems due to GBS: 1

Table 2: Maternity professionals focus group participant characteristics

Focus group number	Number of participants	Participant characteristics (including any additional information specified by participant)
1	9	• All midwives • Additional specified roles: 4 research midwives, 1 midwife/sonographer, 1 community/research midwife
2	2	• Both community midwives • 1 trains other midwives about influenza vaccine
3	10	• Obstetric doctors
4	7	• Obstetric doctors, one consultant, remainder in obstetric training posts

Table 3: Suggested methods for encouraging participation in GBS vaccine trials

Pregnant women/GBS experienced	Maternity professionals
Offer opportunity to speak with a parent affected by GBS (not all would want this)	Offer extra ultrasound scans
Invited to take part by their own midwife	Offer opportunity to speak with a parent affected by GBS
Enthusiasm and support from their own midwife	Midwives to be involved in recruitment (obstetric doctor group only)
Extra appointments/attention	Using patient advocates (e.g. GBS experienced parents) to promote the trial to maternity professionals
Flexible evening and weekend appointments	Possible financial incentive/free nappies
An emphasis on protection for their own baby	
An emphasis on the altruistic benefit to others	

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